REMARKS

Claims 1, 6-12 and 25-33 were pending in the application. Claim 1 has been amended. Claims 25-33 have been canceled. Accordingly, upon entry of the amendments presented herein, claims 1 and 6-12 will be pending in the application.

Claim 1 has been amended to specify a complex comprising full length monomeric IgA linked to an agent. Support for this amendment can be found in the present specification, at least, for example, at page 3, lines 1-2; page 3, lines 28-32; page 3, line 37 through page 4, line 2; page 8, lines 25-26; page 13, lines 1-7; page 14, lines 22-25; page 14, lines 30-33 of the specification as originally filed; and original claim 3.

The foregoing amendments should in no way be construed as acquiescence to any of the Examiner's rejections, and have been made solely to expedite examination of the present application and to place the pending claims in better condition for appeal. No new issues have been raised and no additional search should be required. Accordingly, Applicants respectfully request that the foregoing claim amendments be entered. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s). *No new matter has been added.*

Objection to the Specification

At paragraph 8 of the pending Office Action, the Examiner objects to Applicant's amendment to the specification filed on April 1, 2003 as introducing new matter. Specifically, the Examiner asserts that the amendment to incorporate by reference U.S. Provisional Application No. 60/192,727 into the specification is improper because "a priority application cannot be incorporated by reference after the original filing of the instant application."

Applicant notes that the priority claim to U.S. Provisional Application No. 60/192,727 was originally made at the time the present application was filed on March 27, 2001 (see original Declaration, Power of Attorney document). Applicant understands that the Examiner is not denying Applicant's priority claim to U.S. Provisional Application No. 60/192,727, but merely objects to the later-added "incorporation by reference" statement included in Applicant's response dated April 1, 2003. Accordingly, as requested by the Examiner, Applicant has amended the specification to remove the incorporation by reference statement,

thereby rendering this objection moot. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw this objection.

At paragraph 9 of the pending Office Action, the Examiner also objects to several minor typographical errors. Applicant has amended the specification to correct typographical errors, thereby rendering this objection moot. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw this objection.

Rejection of Claims 1, 6, 8 and 11-12 Under 35 U.S.C. § 102(b)

Claims 1, 6, 8 and 11-12 are rejected under 35 U.S.C. § 102(b) as being anticipated by Mannhalter *et al.* (U.S. Patent 5,808,000, issued 9/15/1998). Specifically, the Examiner asserts that claim 1 is anticipated by Mannhalter *et al.* because it "only requires monomeric IgA to be linked by chemical conjugation or recombinant genetic fusion, not the 'portion thereof that binds to FcαRI." Additionally, the Examiner argues that even if claim 1 was amended to indicate that the "portion" is linked to an agent, "Mannhalter *et al.* would still apply since monomeric IgA assembly occurs by genetic recombination of immunoglobulin genes *in vivo*, which is merely one interpretation of genetic fusion."

Applicant respectfully traverses the foregoing rejection. However, to expedite prosecution, claim 1 has been amended to delete reference to "portions" of monomeric IgA. Mannhalter *et al.* neither teach nor suggest chemically linking monomeric IgA to another molecule, nor fusing such molecules by *ex vivo* genetic recombination. Accordingly, this rejection is moot.

Rejection of Claims 1, 6 8-11, 26-27, and 29-32 Under 35 U.S.C. § 102(b)

Claims 1, 6, 8-11, 26-27 and 29-32 are rejected under 35 U.S.C. § 102(b) as being anticipated by van Spriel *et al.* (*Journal of Infectious Diseases*, 179(3):661-669, 3/3/1999) as evidenced by Van Egmond *et al.* (*Nature Medicine*, 6(6):68-685, June 2000). While the Examiner acknowledges that "van Spriel do not teach monomeric IgA," the Examiner alleges that a portion of monomeric IgA that binds to FcαRI "broadly reads on an anti-FcαRI Fab linked to a *C. albicans* directed F(ab')2 as taught by the prior art...since a Fab fragment is a 'portion' of monomeric IgA."

Applicant respectfully traverses this rejection. However, as described above, independent claim 1 has been amended without prejudice to delete reference to "portions" of

monomeric IgA. van Spriel *et al.* fail to teach or suggest using monomeric IgA as presently claimed. Thus, the pending claims are novel over this cited reference and the rejection is moot.

Rejection of Claims 1, 6-12 and 26-33 Under 35 U.S.C. § 102(e)

Claims 1, 6-12 and 26-33 are rejected under 35 U.S.C. § 102(e) as being anticipated by Deo *et al.* (U.S. Patent 5,922,845, filed 7/11/1996) as evidenced by Van Egmond *et al.* (*Nature Medicine*, 6(6):68-685, June 2000). While the Examiner acknowledges that Deo *et al.* do not teach monomeric IgA, the Examiner is of the opinion that a portion of monomeric IgA that binds to FcαRI "broadly reads on the administration of an antigen-binding antibody fragment (i.e. Fab Fab', $F(ab)_2$, Fv or single chain Fv) that binds to FcαRI linked to an antibody or antigen-binding fragment thereof (i.e., 'an agent') that binds to a bacteria, virus, fungi or cancer cell as taught by Deo et al."

Applicant respectfully traverses the foregoing rejection. To expedite prosecution, independent claim 1 has been amended without prejudice to delete reference to "portions" of IgA. Deo *et al.* fail to teach monomeric IgA, let alone the use of monomeric IgA as presently claimed. Accordingly, the claims are novel over this cited reference and the rejection is moot.

Rejection of Claims 1, 6-12 and 25-33 Under 35 U.S.C. § 112, First Paragraph

Claims 1, 6-12 and 25-33 are rejected under 35 U.S.C. § 112, first paragraph, as introducing new matter. Specifically, the Examiner is of the opinion that "[t]he disclosure of a first portion that targets FcαRI or monomeric IgA or the Fc region thereof does not provide adequate written support for a first portion of the molecular complex that is monomeric IgA or portion thereof that binds to FcαRI as presently claimed."

Applicant respectfully traverses this rejection. From the outset of the specification (see, for example, the first paragraph of the Summary of the Invention at page 2, lines 20-26), Applicant makes it clear that the invention is based on the discovery that monomeric (serum) IgA binds to FcαR-expressing cells and causes elimination (*e.g.*, phagocytosis) of antigens bound to monomeric IgA. Accordingly, it is the focus of this application to harness this feature of monomeric IgA to eliminate a target cell or antigen from the circulatory system of

a subject, as currently claimed. Therefore, the use of monomeric IgA within the claimed complexes is clearly contemplated within the four corners of the present specification.

In particular, the specification teaches that such methods for eliminating a target cell or antigen include the use of a complex which has a first portion that binds FcαRI expressed on Kupffer cells. As further taught in the specification, the first portion includes various molecules, such as monomeric IgA itself or molecules which bind to monomeric IgA; see, for example, page 3, lines 1-6, which state that "[i]n a particular embodiment of the invention, the first portion of the complex comprises serum (monomeric) IgA . . . In another embodiment, the first portion of the complex comprises an antibody, or fragment thereof, which specifically binds FcαRI or which specifically binds monomeric IgA . . ." (emphasis added).

Further evidence that monomeric IgA itself, as claimed, is supported by the present specification is provided, for example, at the following locations where Applicant refers to monomeric IgA as the first portion of the complex that "binds FcαRI"

- page 3, lines 28-32;
- page 3, line 37 through page 4, line 2;
- page 14, lines 22-25; and page 14, lines 30-33.

Moreover, original claim 3 explicitly recites that "the first portion of the complex comprises monomeric IgA."

Based at least on the foregoing, it is clear that no new matter has been introduced and the pending claims are fully supported by the specification.

The Examiner further states that the specification "criticizes and discourages the use of monomeric IgA" and concludes that that one of ordinary skill in the art "would not have been led to the claimed method of administering a complex comprising monomeric IgA...in view [of the fact] that serum IgA may interfere with the activity of such a complex under physiological conditions and the disclosure of using a complex that binds at a site on a FcαR that is distinct from the binding site for IgA, so that binding of the complex is not blocked by endogenous IgA."

Applicant respectfully traverses this rejection. As described above, the use of monomeric IgA in the presently claimed methods is clearly described and supported. The fact that other alternative embodiments are also taught within the specification does not nullify actual support for the claimed invention.

With respect to the Examiner's objection to the lack of working examples which involve administration of monomeric IgA, as claimed, Applicant respectfully disagree. As described in the present specification (see, *e.g.*, page 6, lines 24-33; the Examples at pages 15-21; and the figures) data is provided which exemplify that monomeric IgA mediate phagocytosis via FcαRI and, therefore, the present specification shows that monomeric IgA-FcαRI interactions on Kupffer cells provide a second line of defense at the interface of mucosal and systemic immunity by eliminating invasive bacteria entering via the portal circulation.

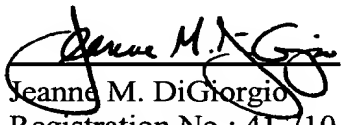
Based on Applicant's teachings in the specification, one of ordinary skill in the art would recognize that Applicant was in possession of the claimed invention. Accordingly, since the subject matter of the pending claims is described in accordance with 35 U.S.C. §112, first paragraph, Applicant respectfully requests that the Examiner reconsider and withdrawn the foregoing rejection.

CONCLUSION

In view of the above amendments and remarks set forth above, it is respectfully submitted that this application is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with Applicants' Attorney could be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

Dated: November 13, 2006

Respectfully submitted,



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